

WHAT IS CLAIMED IS:

1. A protein comprising any amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence represented by SEQ ID No:1;
  - (b) an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein consists of an amino acid sequence having a homology of 85% or more with the amino acid sequence represented by SEQ ID No:1;
  - (c) the amino acid sequence represented by SEQ ID No:25;
  - (d) the amino acid sequence represented by SEQ ID No:26;
  - (e) an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises the amino acid sequence of the amino acid Nos.96 to 126 of SEQ ID No:1;
  - (f) an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises an amino acid sequence having a homology of 95% or more with the amino acid sequence of the amino acid Nos.96 to 126 of SEQ ID No:1;
  - (g) an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises at its N-terminal the amino acid sequence of the amino acid Nos.1 to 126 of SEQ ID No:1; and
  - (h) an amino acid sequence of a protein involved in a G

protein-coupled receptor mediated signal transduction, said protein comprises at its N-terminal an amino acid sequence having a homology of 65% or more with the amino acid sequence of the amino acid Nos.1 to 126 of SEQ ID No:1.

2. A protein (1) or (2):

(1) the protein consisting of the amino acid sequence represented by SEQ ID No:1;

(2) a protein involved in a G protein-coupled receptor mediated signal transduction which consists of an amino acid sequence having a homology of 85% or more with the amino acid sequence represented by SEQ ID No:1.

3. The protein consisting of the amino acid sequence represented by SEQ ID No:25.

4. The protein consisting of the amino acid sequence represented by SEQ ID No:26.

5. A protein (3) or (4):

(3) a protein involved in a G protein-coupled receptor mediated signal transduction which comprises the amino acid sequence of the amino acid Nos.96 to 126 of SEQ ID No:1;

(4) a protein involved in a G protein-coupled receptor mediated signal transduction which comprises an amino acid sequence having a homology of 95% or more with the amino acid sequence of the amino acid Nos.96 to 126 of SEQ ID No:1.

6. A protein (5) or (6):

(5) a protein involved in a G protein-coupled receptor mediated signal transduction which comprises at its N-terminal the amino acid sequence of the amino acid Nos.1 to 126 of SEQ ID No:1;

(6) a protein involved in a G protein-coupled receptor mediated signal transduction which comprises at its N-terminal an amino acid sequence having a homology of 65% or more with the amino acid sequence of the amino acid Nos.1 to 126 of SEQ ID No:1.

7. A polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding the amino acid sequence represented by SEQ ID No:1;

(b) a nucleotide sequence encoding an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein consists of an amino acid sequence having a homology of 85% or more with the amino acid sequence represented by SEQ ID No:1;

(c) a nucleotide sequence encoding the amino acid sequence represented by SEQ ID No:25;

(d) a nucleotide sequence encoding the amino acid sequence represented by SEQ ID No:26;

(e) a nucleotide sequence encoding an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises the

amino acid sequence of the amino acid Nos.96 to 126 of SEQ ID No:1;

(f) a nucleotide sequence encoding an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises an amino acid sequence having a homology of 95% or more with the amino acid sequence of the amino acid Nos.96 to 126 of SEQ ID No:1;

(g) a nucleotide sequence encoding an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises at its N-terminal the amino acid sequence of the amino acid Nos.1 to 126 of SEQ ID No:1;

(h) a nucleotide sequence encoding an amino acid sequence of a protein involved in a G protein-coupled receptor mediated signal transduction, said protein comprises at its N-terminal an amino acid sequence having a homology of 65% or more with the amino acid sequence of the amino acid Nos.1 to 126 of SEQ ID No:1;

(i) the nucleotide sequence represented by SEQ ID No:2;

(j) a nucleotide sequence of a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide consists of a nucleotide sequence having a homology of 85% or more with the polynucleotide consisting of the nucleotide sequence

represented by SEQ ID No:2;

(k) the nucleotide sequence represented by SEQ ID No:27;

(l) the nucleotide sequence represented by SEQ ID No:28;

(m) a nucleotide sequence of a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises the nucleotide sequence of the nucleotide Nos.289 to 378 of SEQ ID No:2;

(n) a nucleotide sequence of a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises a nucleotide sequence having a homology of 90% or more with the polynucleotide consisting of the nucleotide sequence of the nucleotide Nos.289 to 378 of SEQ ID No:2;

(o) a nucleotide sequence of a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises at its 5' terminal the nucleotide sequence of the nucleotide Nos.1 to 378 of SEQ ID No:2; and

(p) a nucleotide sequence of a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises at its 5' terminal a nucleotide sequence having a homology of 70% or more with the polynucleotide consisting of the nucleotide sequence of the nucleotide Nos.1 to 378 of SEQ

ID No:2.

8. A polynucleotide of (7) or (8):

(7) the polynucleotide consisting of the nucleotide sequence represented by SEQ ID No:2;

(8) a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide consists of a nucleotide sequence having a homology of 85% or more with the polynucleotide consisting of the nucleotide sequence represented by SEQ ID No:2.

9. The polynucleotide consisting of the nucleotide sequence represented by SEQ ID No:27.

10. The polynucleotide consisting of the nucleotide sequence represented by SEQ ID No:28.

11. A polynucleotide of (9) or (10):

(9) a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises the nucleotide sequence of the nucleotide Nos.289 to 378 of SEQ ID No:2;

(10) a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises a nucleotide sequence having a homology of 90% or more with the polynucleotide consisting of the nucleotide sequence of the nucleotide Nos.289 to 378 of SEQ ID No:2.

12. A polynucleotide of (11) or (12):

(11) a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises at its 5' terminal the nucleotide sequence of the nucleotide Nos.1 to 378 of SEQ ID No:2;

(12) a polynucleotide encoding a protein involved in a G protein-coupled receptor mediated signal transduction, said polynucleotide comprises at its 5' terminal a nucleotide sequence having a homology of 70% or more with the polynucleotide consisting of the nucleotide sequence of the nucleotide Nos.1 to 378 of SEQ ID No:2.

13. A recombinant vector containing a polynucleotide according to Claim 7.

14. A method for producing a recombinant vector comprising a step for integrating a polynucleotide according to Claim 7 into a vector capable of being replicated in a host cell.

15. A transformant having a recombinant vector according to claim 13.

16. A method for producing a transformant comprising a step for transducing a recombinant vector according to claim 13 into a host cell.

17. A method for producing a G protein  $\alpha$ -subunit comprising steps for culturing a transformant having a recombinant vector containing a polynucleotide according to Claim 7 and recovering from the culture a protein resulting

from the polynucleotide according to Claim 7.

18. An antisense polynucleotide consisting of a polynucleotide of (13) or (14):

(13) a polynucleotide which inhibits the expression of a protein according to Claim 1 which comprises a nucleotide sequence complementary to at least 15 contiguous nucleotides in the nucleotide sequence represented by SEQ ID No:2;

(14) a polynucleotide which inhibits the expression of a protein according to Claim 1 which hybridizes under an intracellular condition with a polynucleotide consisting of at least 15 contiguous nucleotides in the nucleotide sequence represented by SEQ ID No:2.

19. A ribozyme (15) or (16):

(15) a ribozyme having an ability of cleaving a polynucleotide according to Claim 7 which comprises two polynucleotide regions complementary to two regions respectively consisting of at least 9 contiguous nucleotides which are two regions in the nucleotide sequence represented by SEQ ID No:2;

(16) a ribozyme having an ability of cleaving a polynucleotide according to Claim 7 which comprises two polynucleotide regions which hybridizes under an intracellular condition with two regions respectively consisting of at least 9 contiguous nucleotides which are



two regions in the nucleotide sequence represented by SEQ ID No:2.

20. An antibody which recognizes a protein according to Claim 1 specifically.

21. An agent for regulating a G protein-coupled receptor mediated signal transduction containing as an active ingredient a protein according to Claim 1.

22. A therapeutic or prophylactic agent against a disease caused by a G protein-coupled receptor mediated signal transduction abnormality, wherein an active ingredient of the agent is a protein according to Claim 1.

23. An agent for regulating a G protein-coupled receptor mediated signal transduction containing as an active ingredient a polynucleotide according to Claim 7.

24. A therapeutic or prophylactic agent against a disease caused by a G protein-coupled receptor mediated signal transduction abnormality, wherein an active ingredient of the agent is a polynucleotide according to Claim 7.

25. An agent for regulating a G protein-coupled receptor mediated signal transduction containing as an active ingredient an antisense polynucleotide according to Claim 18.

26. A therapeutic or prophylactic agent against a disease caused by a G protein-coupled receptor mediated

signal transduction abnormality, wherein an active ingredient of the agent is an antisense polynucleotide according to Claim 18.

27. An agent for regulating a G protein-coupled receptor mediated signal transduction containing as an active ingredient a ribozyme according to Claim 19.

28. A therapeutic or prophylactic agent against a disease caused by a G protein-coupled receptor mediated signal transduction abnormality, wherein an active ingredient of the agent is a ribozyme according to Claim 19.

29. An agent for regulating a G protein-coupled receptor mediated signal transduction containing as an active ingredient an antibody according to Claim 20.

30. A therapeutic or prophylactic agent against a disease caused by a G protein-coupled receptor mediated signal transduction abnormality, wherein an active ingredient of the agent is an antibody according to Claim 20.

31. An oligonucleotide (17) or (18):

(17) an oligonucleotide capable of recognizing a polynucleotide represented by SEQ ID NO:2 specifically which consists of at least 17 contiguous nucleotides in the nucleotide sequence represented by SEQ ID No:2;

(18) an oligonucleotide capable of recognizing a polynucleotide represented by SEQ ID NO:2 specifically

which has a homology of 80% or more with at least 17 contiguous nucleotides in the nucleotide sequence represented by SEQ ID No:2.

32. An oligonucleotide according to Claim 31 which is used as a probe or a primer.

33. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

(a) a step for bringing a test substance into contact with a test cell having a recombinant vector according to Claim 13 and a recombinant vector containing a DNA encoding a G protein-coupled receptor protein;

(b) a step for measuring the G protein effector activity or the index value correlating therewith in the test cell; and

(c) a step for comparing this effector activity or the index value correlating therewith with the effector activity or the index value correlating therewith in the test cell which has not been brought into contact with the test substance, whereby selecting a test substance capable of altering the effector activity or the index value correlating therewith in the test cell.

34. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

(a) a step for bringing a test substance into contact with

a test cell having a recombinant vector according to Claim 13 and a recombinant vector containing a DNA encoding a G protein-coupled receptor protein;

(b) a step for measuring the G protein effector activity or the index value correlating therewith in the test cell; and

(c) a step for comparing this effector activity with the effector activity or the index value correlating therewith when the said test substance has been brought into contact with a control cell having no recombinant vector according to Claim 13 but having a recombinant vector containing a DNA encoding a G protein-coupled receptor protein, whereby selecting a test substance causing a difference in the effector activity or the index value correlating therewith between the test cell and the control cell.

35. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

(a) a step for bringing a test substance into contact with a test cell having a recombinant vector according to Claim 13 and a recombinant vector containing a DNA encoding a G protein-coupled receptor protein;

(b) a step for measuring the G protein effector activity or the index value correlating therewith in the test cell; and

(c) a step for comparing this effector activity or the index value correlating therewith with the effector

activity or the index value correlating therewith when the said test substance has been brought into contact with a control cell having no recombinant vector containing a DNA encoding a G protein-coupled receptor protein but having a recombinant vector according to Claim 13, whereby selecting a test substance causing a difference in the effector activity or the index value correlating therewith between the test cell and the control cell.

36. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

- (a) a step for bringing a test substance and a G protein-coupled receptor ligand into contact with a test cell having a recombinant vector according to Claim 13 and a recombinant vector containing a DNA encoding a G protein-coupled receptor protein;
- (b) a step for measuring the G protein effector activity or the index value correlating therewith in the test cell; and
- (c) a step for comparing this effector activity or the index value correlating therewith with the effector activity or the index value correlating therewith in the test cell which has not been brought into contact with the test substance but has been brought into contact with the ligand, whereby selecting a test substance capable of altering the effector activity or the index value

correlating therewith in the test cell.

37. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

- (a) a step for bringing a test substance and a G protein-coupled receptor ligand into contact with a test cell having a recombinant vector according to Claim 13 and a recombinant vector containing a DNA encoding a G protein-coupled receptor protein;
- (b) a step for measuring the G protein effector activity or the index value correlating therewith in the test cell;
- (c) a step for comparing this effector activity with the effector activity in the test cell which has not been brought into contact with the test substance but has been brought into contact with the ligand, whereby investigating the change in the effector activity in the test cell; and
- (d) a step for comparing the rate of change in this effector activity or the index value correlating therewith with the rate of change in the effector activity or the index value correlating therewith when the said test substance and said ligand has been brought into contact with a control cell having no recombinant vector containing a DNA encoding a G protein-coupled receptor protein but having a recombinant vector according to Claim 13, whereby selecting a test substance causing a difference in the rate

of change in the effector activity or the index value correlating therewith between the test cell and the control cell.

38. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

(a) a step for bringing a test substance into contact with a cell membrane fraction of a cell having a recombinant vector according to Claim 13 and a cell membrane fraction of a cell having a recombinant vector containing a DNA encoding a GPCR, or

a cell membrane fraction of a cell having the recombinant vector according to Claim 13 and the recombinant vector containing the DNA encoding the GPCR;

(b) a step for assaying the level of the binding of GTP to the cell membrane fraction; and

(c) a step for comparing the assayed level of this GTP binding with the assayed level of the GTP binding to the cell membrane fraction which has not been brought into contact with the test substance, whereby selecting a test substance capable of altering the assayed level of the GTP binding to the cell membrane fraction.

39. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

(a) a step for bringing a test substance and a G protein-coupled receptor ligand into contact with a cell membrane fraction of a cell having a recombinant vector according to Claim 13 and a cell membrane fraction of a cell having a recombinant vector containing a DNA encoding a GPCR, or a cell membrane fraction of a cell having the recombinant vector according to Claim 13 and the recombinant vector containing the DNA encoding the GPCR;

(b) a step for assaying the level of the binding of GTP to the cell membrane fraction; and

(c) a step for comparing the assayed level of this GTP binding with the assayed level of the GTP binding in the cell membrane fraction which has not been brought into contact with the test substance but has been brought into contact with said ligand, whereby selecting a test substance capable of altering the assayed level of the GTP binding to the cell membrane fraction.

40. A method for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein comprising:

(a) a step for bringing a test substance into contact with a test cell capable of expressing a protein according to Claim 1;

(b) a step for measuring the expression level of the



protein according to Claim 1 in the test cell; and  
(c) a step for comparing this expression level with the expression level of said protein in the test cell which has not been brought into contact with the test substance, whereby selecting a test substance capable of altering the expression level of said protein in the test cell.

41. A substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a G protein, said substance is obtained by a screening method according to any of Claims 33 to 40.

42. An agent for regulating a signal transduction mediated by a G protein-coupled receptor and a G protein, said agent contains as an active ingredient a substance according to Claim 41.

43. A therapeutic or prophylactic agent against a disease caused by the abnormality in a G protein-coupled receptor and a G protein-mediated signal transduction containing as an active ingredient a substance according to Claim 41.

44. A kit for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a protein according to Claim 1, which comprises a test cell having a recombinant vector containing a polynucleotide encoding a protein according to Claim 1 and a reagent for measuring the G protein effector

activity or an index value correlating therewith.

45. A screening kit according to Claim 44 wherein the test cell further has a recombinant vector having a DNA encoding a G protein-coupled receptor.

46. A screening kit according to Claim 44 further containing a G protein-coupled receptor ligand.

47. A screening kit according to Claim 44 further containing a control cell having a recombinant vector having a DNA encoding a G protein-coupled receptor.

48. A screening kit according to Claim 44 further containing a control cell having a recombinant vector containing a polynucleotide encoding a protein according to Claim 1.

49. A kit for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a protein according to Claim 1, which comprises:

a cell having a recombinant vector containing a polynucleotide encoding a protein according to Claim 1; and,

a GTP analogue which can bind to the protein according to Claim 1 but can not be cleaved by a GTPase.

50. A screening kit according to Claim 49 wherein the cell further has a recombinant vector having a DNA encoding a G protein-coupled receptor.

51. A kit for screening for a substance capable of

regulating a signal transduction mediated by a G protein-coupled receptor and a protein according to Claim 1, which comprises:

- a cell having a recombinant vector containing a polynucleotide encoding a protein according to Claim 1;

- a cell having a recombinant vector having a DNA encoding the G protein-coupled receptor; and,

- a GTP analogue which can bind to the protein according to Claim 1 but can not be cleaved by a GTPase.

52. A screening kit according to Claim 49 or 51 further containing a G protein-coupled receptor ligand.

53. A kit for screening for a substance capable of regulating a signal transduction mediated by a G protein-coupled receptor and a protein according to Claim 1, which comprises:

- a cell capable of expressing a protein according to Claim 1; and

- an oligonucleotide according to Claim 31 or an antibody according to Claim 20.